REMARKS

Claims 1-104 are pending. Claims 60, 65, 66, 84-88, and 90 are under examination. Applicants respectfully request reconsideration of the claims in view of the Remarks below in conjunction with those previously of record.

Rejection under 35 U.S.C. §103

The rejection of claims 60, 65, 84, 87, and 90 under 35 U.S.C. §103(a) as allegedly being obvious over King et al. (caplus an 1993:212888) is respectfully traversed.

Applicants remarks to the previous Office Action are incorporated herein. Applicants reiterate that the Examiner has failed to present a *prima facie* case of obviousness under the standards of current case law. The Examiner is deficient in showing a *prima facie* case of obviousness because 1) there was inadequate reasoning presented by the Examiner as to why one skilled in the art would be motivated to use the compound as taught by King et al. as a lead compound for the discovery of the species identified within the claimed genus and 2) the Examiner failed to provide a reason why the skilled chemist would have been motivated to alter the King et al. compound in a particular manner to arrive at the member of the claimed genus. The Federal Circuit has opined on the obviousness of chemical compounds in numerous decisions post-KSR and the following excerpt details what is required in establishing a *prima facie* case of obviousness, in particular:

> "An obviousness argument based on structural similarity between claimed and prior art compounds 'clearly depends on a preliminary finding that **one of ordinary skill in the art would have selected [the prior art compound] as a lead compound**.'" *The Proctor and Gamble Company v. Teva Pharmaceuticals USA, Inc.* Case Nos. 08-1404, -1405, -1406 (Fed. Cir., May 13, 2009) quoting Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd., 492, F.3d at 1359 (Fed. Cir. 2007). emphasis added
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> "it remains necessary to identify **some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness** of a new claimed compound." Takeda 492 F.3d at 1350, 1357, emphasis added.

In response to the Applicants arguments, the Examiner alleges that the identified compound in King et al. has pharmacological activity. Applicants respectfully disagree that this

alone would have led someone skilled in the art to select the compound taught by King et al. as a lead compound. The compound taught by King et al. is described as being useful for the treatment of headache, including migraine. By contrast, the present invention is directed to compounds for viral inhibition. Therefore, there is no motivation whatsoever for a skilled artisan to select the compound taught by King et al. as a starting point to develop viral inhibitors.

The Examiner's implication that because the compound taught by King et al. possesses *any* pharmacological activity provides sufficient motivation to select it as a lead compound ignores the enormous disparity in the observed biological activity profiles for these two compounds. Moreover, given the high degree of unpredictability of the pharmacological sciences, the Examiner's allegation that a positional isomer would be expected to possess *any* pharmacological activity is tenuous at best, and appears to be the result of hindsight knowledge that the claimed compound coincidentally did display *some kind* of pharmacological activity. For example, one skilled in the art will recognize that a change in position of a substituent in a molecule frequently makes the difference between binding and not binding to a biological target.

Even assuming *arguendo* that one were to select the compound taught by King et al., the Examiner would further need to identify a reason for making the particular structural changes necessary to arrive at the claimed compound. The Examiner is silent in this regard, relying only on standards set forth in the MPEP that might be more appropriately applied outside of a pharmacological context comparing the properties of, for example, *n*-pentane to *iso*-pentane.

Finally, Applicants wish to clarify the record with respect to the Examiner's Response to Applicants Arguments. The Examiner appears to dismiss the differences in physical and chemical properties as not relevant in view of the fact that the King et al compound possesses pharmacological activity. Applicants wish to point out that such physical and chemical properties are at the heart of interactions of small molecules with biological targets and whether or not there will be *any* pharmacological activity. Alterations in the electronics and steric environment can dramatically alter a critical binding event in a biological context, for example. Such changes are frequently unpredictable even in the presence of detailed binding models of the target.

Applicants assert that claims 60, 65, 84, 87, and 90 are all patentable over King et al. for at least these reasons and respectfully request withdrawal of this rejection.

In light of the remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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